(b) a nucleic acid sequence degenerate to a sequence of (a) as a result of the genetic code.

65. (New) An isolated nucleic acid molecule encoding an odorant receptor protein comprising seven transmembrane domains and a 17-amino acid cytoplasmic loop between the fifth and sixth transmembrane domains, wherein the nucleic acid molecule comprises:

B5

(a) a nucleic acid sequence given in any one of the Figures 19 to 31 (SEQ ID NOs.: 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, or 35); or

(b) a nucleic acid sequence degenerate to a sequence of (a) as a result of the genetic code.

REMARKS

Claims 1-24 are pending and under examination in the subject application. Applicants have amended claims 1, 6 and 8 in order to introduce certain format changes. Support for the 17-amino acid cytoplasmic loop between the fifth and sixth transmembrane domains, can be found in the specification at, *inter alia*, page 40, line 9 and figures 4I, 5, and 6A(2)-6A(4). Applicants maintain that these amendments raise no issue of new matter. Additionally, applicants add new claim 64 and 65. Support for new claim 64 can be found in, *inter alia*, Figures 9-18. Support for new claim 65 can be found in, *inter alia*, Figures 19-31. Additionally, applicants have

canceled claims 9-12 without prejudice. Upon entry of this Amendment, claims 1-8, 13-24, 64 and 65 will be pending and under examination.

Pursuant to the requirements of 37 C.F.R. 1.121(c)(1)(ii), applicants annex hereto as **Exhibit B** claims 1, 6 and 8 marked up to show the changes made herein relative to the previous version of those claims.

In view of the arguments set forth below, applicants maintain that the Examiner's objections and rejections made in the July 11, 2002 Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

The Claimed Invention

This invention provides nucleic acid molecules encoding odorant receptor proteins and related embodiments. These odorant receptors are members of a large superfamily of surface receptors which all traverse the membrane seven times. However, these odorant receptors are distinguished from the other surface receptors by the specialized role they play in olfactory perception.

Objection under 37 C.F.R. §1.75(c)

The Examiner objected to claim 20 under 37 C.F.R. 1.75(c), as allegedly of improper dependent form for failing to further limit the subject matter of a previous claim.

Specifically, the Examiner asserted that claim 20 can be infringed by a polypeptide composition which does not infringe the nucleic acid composition of any of the claims from which claim 20 depends.

In response, applicants respectfully traverse the Examiner's objection, maintaining that claim 20 satisfies the requirements of 37 C.F.R. §1.75(c). Nevertheless, should the Examiner maintain the objection, applicants will amend claim 20 to place it in independent form.

Noncompliance of Drawings under 37 C.F.R. §1.821(d)

The Examiner rejected the drawings in the instant application for noncompliance with 37 C.F.R. §1.821(d), which requires a reference to a particular sequence identifier be made in the specification and claims wherever a reference is made to that sequence.

Specifically, the Examiner asserted that sequence identifiers were not used in those drawings where sequences were presented, nor included in the Brief Description of the Drawings.

In response, applicants submit herewith a Sequence Listing attached hereto as **Exhibit C**. In addition, applicants submit herewith a computer diskette, whose contents are identical to those of the paper copy attached as Exhibit C. A Statement of Compliance stating that the contents of the computer readable form and the paper copy submitted herewith are identical is attached hereto as **Exhibit D**. The new Sequence Listing complies with the requirements

of 37 C.F.R. §1.823 and does not contain any new matter.

Applicants have also amended the Brief Description of the Drawings to recite the required sequence identifiers of sequences appearing in the drawings.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1-24 under 35 U.S.C. §112, first paragraph, as allegedly not providing an adequate written description of a DNA encoding an odorant receptor lacking the entire amino acid sequence of any of the twenty-three amino acid sequences which are disclosed in the instant application.

Specifically, the Examiner asserted that "the instant specification does not provide a structural formula which is definitive of *all* odorant receptors" [emphasis added].

In response to the rejection of claims 9-12, applicants point out that these claims have been canceled, making the rejection thereof moot.

In response to the rejection of claims 1-8 and 13-24, applicants respectfully traverse. Applicants note that the instant claims are drawn to nucleic acids encoding odorant receptors having defined physical features, namely seven transmembrane domains and a 17-amino acid cytoplasmic loop between the fifth and sixth transmembrane domains.

M.P.E.P §2163(II)(A)(3)(a)(ii) states that "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number* of species by actual reduction to practice . . . sufficient to show the applicant was in possession of the claimed genus" [emphasis added]. Applicants maintain that the odorant receptor proteins whose sequences are set forth in the specification constitute a representative number of species of the claimed genus. Thus, applicants maintain that the written description requirement for claims 1-8 and 13-24 is satisfied.

The Examiner also rejected claims 1-24 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or to which it is most nearly connected, to use the invention commensurate in scope with the claims.

Specifically, the Examiner alleges that a claimed odorant receptor protein is meaningless unless the specific ligand or ligands that bind to that receptor are identified. The Examiner alleges that because applicant has not demonstrated the binding of a specific odorant to any one of the disclosed proteins, other than the I7 receptor, the other claimed receptor proteins have no practical utility.

In response to the rejection of claims 9-12, applicants point out that these claims have been canceled, making the rejection thereof

moot.

In response to the rejection of claims 1-8 and 13-24, applicants respectfully traverse. Applicants note that the instant claims are drawn to nucleic acids encoding odorant receptors having defined physical features, namely seven transmembrane domains and a 17-amino acid cytoplasmic loop between the fifth and sixth transmembrane domains.

Applicants maintain that one skilled in the art could make and use the instant nucleic acids encoding the odorant receptor proteins whose sequences are set forth in the specification. Thus, applicants maintain that the enablement requirement for claims 1-8 and 13-24 is satisfied.

The Examiner further rejected claims 1-24 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is nearly connected, to make the invention commensurate in scope with the instant claims.

Specifically, the Examiner asserts that while twenty-three odorant receptor amino acid sequences were disclosed in the instant specification, the scope of the claims encompass odorant receptor proteins encoded by something other than the amino acid sequences described therein. Additionally, the Examiner asserts that the claims allow the amino acid sequence of an odorant receptor recited

therein to deviate substantially from each of the twenty-three naturally occurring proteins described therein.

In response to the rejection of claims 9-12, applicants point out that these claims have been canceled, making the rejection thereof moot.

In response to the rejection of claims 1-8 and 13-24, applicants respectfully traverse the Examiner's rejection. The Examiner himself cites *In re Fisher*, 427 F.2d. 833, 166 USPQ 18 (CCPA 1970), wherein it states, "[i]nventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work."

In the instant application, applicants claim only the invention based on their teachings or made possible by their work. On page 7, line 29-31, the specification states, "[h]owever, all of the proteins shown here share sequence motifs not found in other members of this superfamily and are clearly members of a novel family of proteins." The instant claims encompass those later embodiments which incorporate or derive from the common sequence motifs or specific nucleotide sequences discovered by applicants.

In view of the above remarks, applicants maintain that claims 1-8 and 13-24 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §102(b)

The Examiner rejected claims 1-24 under 35 U.S.C. §102(b), as allegedly anticipated by Zhao et al.

Specifically, the Examiner asserts that applicants have lost their right to patent under 35 U.S.C. §102(b) because the Zhao et al. article was published in January 1998, more than one year prior to the date of filing of the instant application.

In order to sustain his §102(b) rejection, the Examiner asserts that, under 35 U.S.C. §120, the instant application is not entitled to the benefit of the priority date of the earlier application. The Examiner further states that the instant application can only receive the benefit of the earlier application if it meets the requirements of 35 U.S.C. §112, first paragraph, with respect to the now-claimed invention.

In response to the rejection of claims 9-12, applicants point out that these claims have been canceled, making the rejection thereof moot.

In response to the rejection of claims 1-8 and 13-24 and which applicants understand to apply to new claims 64 and 65, applicants respectfully traverse the Examiner's rejection, and assert that the subject matter of pending claims 1-8, 13-24, and of new claim 64 are fully disclosed by the specification contained in U.S. Patent Application No. 07/681,880, filed April 5, 1991, for which these

claims assert their priority date. Furthermore, the subject matter of new claim 65 is fully disclosed in U.S. Serial No. 08/129,079, filed October 5, 1993.

The following sets forth the location of support for the rejected claims in the specification of U.S. Serial No. 07/681,880. Claims 1-7 are by page 24, line 9 to page 25, line 19, and in Figure 4. Claim 8 is supported on page 17, lines 5-42. Claims 13-15 are supported on page 11, lines 16-18, page 18, lines 9-16, and from page, line 6 to page 21, line 8. Claims 16 and 17 are supported on page 11, lines 3-18. Claims 18 and 19 are supported on page 11, lines 20-27. Claim 20 is supported on page 11, lines 29-35, page 12, lines 1-10, and from page 33, line 28 to page 34, line 17. Claims 22-24 are supported on page 12, lines 12-22. New claim 64 is supported in Figures 9-18.

New claim 65 is supported from page 21, line 7 to page 22, line 25, and from page 32, line 16 to page 33, line 19, and Figures 19 to 31 in U.S. Serial No. 08/129,079.

In view of the remarks above, applicants maintain that claims 1-8, 13-24, and and 64 are entitled to the priority date of U.S. Serial No. 07/681,880, filed April 5, 1991. Furthermore, claim 65 is entitled to the priority date of U.S. Serial No. 08/129,079, filed October 5, 1993. As such, the Zhao et al. article published January 9, 1998 is not prior against the instant claims.

The Examiner also rejected claims 1 to 18 and 20 under 35 U.S.C.

§102(b) as allegedly anticipated by the Buck et al. publication.

Specifically, the Examiner asserts that applicants have lost their right to patent because the Buck et al. article was published on April 5, 1991, more than one year prior to the filing of the instant application.

In response to the rejection of claims 9-12, applicants point out that these claims have been canceled, making the rejection thereof moot.

In response to the rejection of claims 1-8 and 20, applicants respectfully traverse this rejection. For the reasons set forth above, applicants assert that claims 1-18 and 20 are entitled to the priority date of U.S. Serial No. 07/681,880, filed April 5, 1991. As such, the Buck et al. publication is not prior art against these claims.

Furthermore, applicants assert that the Buck et al. publication does not anticipate new claim 65. That particular article provides a written description of an isolated nucleic acid encoding I7, and the protein encoded thereby.

Claim 65 provides a nucleic acid molecule encoding a receptor protein, wherein the nucleic acid has specific sequence-related features. Applicants note that the Buck et al. publication does not teach these features.

Applicants therefore maintain that the Buck et al. publication does not anticipate new claim 65.

In view of the above remarks, applicants maintain that the rejected claims satisfy the requirements of 35 U.S.C. §102(b).

Rejection under 35 U.S.C. §103(a)

The Examiner also rejected claims 19 and 22 to 24 under 35 U.S.C. §103(a) as allegedly unpatentable over the Buck et al. reference published April 5, 1991.

Specifically, the Examiner asserted that it would be *prima facie* obvious to have incorporated a recombinant nucleic acid encoding I7 into an expression vector and host cell to facilitate the possible identification of ligands thereto.

As stated above, applicants maintain that claims 19 and 21 to 24 are entitled to the benefit of the earlier priority date of U.S. Serial No. 07/681,880, filed April 5, 1991. As such, the Buck et al. publication is not prior art against the pending claims.

In view of these above remarks, applicants maintain that the rejected claims satisfy the requirements of 35 U.S.C. §103.

Supplemental Information Disclosure Statement

This Information Disclosure Statement is submitted as a supplement

to the Information Disclosure Statement filed January 26, 2001.

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to Snyder et al. (1989) Trends in NeuroScience 12: 35-38 (**Exhibit 1**). That reference is listed on the attached Form PTO-1449 **(Exhibit E)**, and was cited in a Canadian Search Report, attached hereto as **Exhibit F**, produced in related Canadian Application No. 2,106,847.

No fee, other than the $180 fee required under 37 C.F.R. §1.17(p) for filing the Information Disclosure Statement and the $200.00 fee required for the two-month extension in time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

Respectfully submitted,

I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office on the date indicated below by facsimile and is addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

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Added material is indicated by underlining.

Description of the Figures

Figure 1A-B. The Olfactory Neuroepithelium and a Pathway for Olfactory Signal Transduction.

(A). The Olfactory Neuroepithelium. The initial event in odor perception occurs in the nasal cavity in a specialized neuroepithelium which is diagramed here. Odors are believed to interact with specific receptors on the cilia of olfactory sensory neurons. The signal generated by these initial binding events are propagated by olfactory neuron axons to the olfactory bulb.

(B). A Pathway of Olfactory Signal Transduction. In this scheme, the binding of an odorant molecule to an odor-specific transmembrane receptor leads to the interaction of the receptor with a GTP-binding protein ($G_{s[olf]}$). This interaction, in turn, leads to the release of the GTP-coupled α-subunit of the G-protein, which then stimulates adenylyl cyclase to produce elevated levels of cAMP. The increase in cAMP opens nucleotide-gated cation channels, thus causing an alteration in membrane potential.

Figure 2A-B. A PCR Amplification Product Containing Multiple Species of DNA. cDNA prepared from olfactory epithelium RNA was subjected to PCR amplification with a series of different primer oligonucleotides and the DNA products of appropriate size were isolated, further amplified by PCR, and size fractionated on agarose gels (A) (For details, see text). Each of these semipurified PCR products was digested with the restriction enzyme, Hinf I, and analyzed by agarose gel electrophoresis. Lanes marked "M" contain size markers of 23.1, 9.4, 5.6, 4.4, 2.3, 2.0, 1.35, 1.08, 0.87, 0.60, 0.31, 0.28, 0.23, 0.19, 0.12 and 0.07kb. (B). Twenty-two of the 64 PCR products that were isolated and digested

with Hinf I are shown here. Digestion of one of these, PCR 13, yielded a large number of fragments whose sizes summed to a value much greater than that of the undigested PCR 13 DNA, indicating that PCR 13 might contain multiple species of DNA which are representatives of a multigene family.

Figure 3. Northern Blot Analysis with a Mixture of Twenty Probes. One μg of polyA+ RNA isolated from rat olfactory epithelium, brain, or spleen was size-fractionated in formaldehyde agarose, blotted onto a nylon membrane, and hybridized with a ^{32}P-labeled mixture of segments of 20 cDNA clones. The DNA segments were obtained by PCR using primers homologous to transmembrane domains 2 and 7.

Figure 4A-M. The Protein Sequences Encoded by Ten Divergent cDNA Clones. Ten divergent cDNA clones were subjected to DNA sequence analyses and the protein sequence encoded by each was determined (SEQ ID Nos: 71-80). Amino acid residues which are conserved in 60% or more of the proteins are shaded. The presence of seven hydrophobic domains (I-VII), as well as short conserved motifs shared with other members of the superfamily, demonstrate that these proteins belong to the seven transmembrane (TM) domain protein superfamily. The transmembrane regions are indicated by labeled lines (I-VII) above the sequences. Motifs conserved among members of the family of olfactory proteins include those indicated by underlining below the sequences. In addition, the DRY motif C-terminal to TM3 is common to many members of the G-protein-coupled superfamily. However, all of the proteins shown here share sequence motifs not found in other members of this superfamily and are clearly members of a novel family of proteins.

Figure 5. Positions of Greatest Variability in the Olfactory Protein Family. In this diagram, the protein encoded by cDNA clone

I15 (SEQ ID NO: 6 and SEQ ID NO: 80) is shown traversing the plasma membrane seven times with its N-terminus located extracellularly, and its C-terminus intracellularly. The vertical cylinders delineate the seven putative α-helices spanning the membrane. Positions at which 60% or more of the 10 clones shown in Figure 4 share the same residue as I15 are shown as white balls. More variable residues are shown as black balls. The high degree of variability encountered in transmembrane domains III, IV, and V is evident in this schematic.

Figure 6A-D. The Presence of Subfamilies in a Divergent Multigene Family. Partial nucleotide sequences and deduced protein sequences were obtained for 18 different cDNA clones (SEQ ID Nos: 81-98). Transmembrane domain V along with the flanking loop sequences, including the entire cytoplasmic loop between transmembrane domains V and VI, are shown here for each protein. Amino acid residues found in 60% or more of the clones in a given position are shaded (A). This region of the olfactory proteins (particularly transmembrane domain V) appears to be highly variable (see Figure 4). These proteins, however, can be grouped into subfamilies (B,C,D) in which the individual subfamily members share considerable homology in this divergent region of the protein.

Figure 7. Southern Blot Analyses with Non-crosshybridizing Fragments of Divergent cDNAs. Five μg of rat liver DNA was digested with Eco RI (A) or Hind III (B), electrophoresed in 0.75% agarose, blotted onto a nylon membrane, and hybridized to the ^{32}P-labeled probes indicated. The probes used were PCR-generated fragments of: 1, clone F9 (identical to F12 in Figure 4); 2, F5; 3, F6; 4, I3; 5, I7; 6, I14; or 7, I15. The lane labeled "1-7" was hybridized to a mixture of the seven probes. The probes used showed either no crosshybridization or only trace

crosshybridization with one another. The size markers on the left correspond to the four blots on the left (1-4) whereas the marker positions noted on the right correspond to the four blots on the right (5-7, "1-7").

Figure 8. Northern Blot Analysis with a Mix of Seven Divergent Clones. One μg of polyA+ RNA from each of the tissues shown was size-fractionated, blotted onto a nylon membrane, and hybridized with a ^{32}P-labeled mixture of segments of seven divergent cDNA clones (see Legend to Figure 7).

Figure 9A-D. The nucleic acid and amino acid sequence of clone F3 (SEQ ID NO: 2 and SEQ ID NO: 71, respectively).

Figure 10A-D. The nucleic acid and amino acid sequence of clone F5 (SEQ ID NO: 3 and SEQ ID NO: 72, respectively).

Figure 11A-D. The nucleic acid and amino acid sequence of clone F6 (SEQ ID NO: 4 and SEQ ID NO: 73, respectively).

Figure 12A-D. The nucleic acid and amino acid sequence of clone F12 (SEQ ID NO: 1 and SEQ ID NO: 74, respectively).

Figure 13A-C. Partial nucleic acid and amino acid sequence of clone I3. Full nucleic acid and amino acid sequence of clone I3 are indicated in SEQ ID NO: 7 and SEQ ID NO: 75, respectively.

Figure 14A-D. The nucleic acid and amino acid sequence of clone I7 (SEQ ID NO: 8 and SEQ ID NO: 76, respectively).

Figure 15A-D. The nucleic acid and amino acid sequence of clone I8 (SEQ ID NO: 9 and SEQ ID NO: 77, respectively).

Figure 16A-D. The nucleic acid and amino acid sequence of clone I9 (SEQ ID NO: 10 and SEQ ID NO: 78, respectively).

Figure 17A-D. The nucleic acid and amino acid sequence of clone I14 (SEQ ID NO: 5 and SEQ ID NO: 79, respectively).

Figure 18A-D. The nucleic acid and amino acid sequence of clone I15 (SEQ ID NO: 6 and SEQ ID NO: 80, respectively).

Figure 19A-D. The nucleic acid and amino acid sequence of human clone H5 (SEQ ID NO: 11 and SEQ ID NO: 12, respectively).

Figure 20A-C. The nucleic acid and amino acid sequence of clone J1, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 13 and SEQ ID NO: 14, respectively).

Figure 21A-B. The nucleic acid and amino acid sequence of clone J2 (SEQ ID NO: 15 and SEQ ID NO: 16, respectively).

Figure 22A-B. The nucleic acid and amino acid sequence of clone J4, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 17 and SEQ ID NO: 18, respectively).

Figure 23A-B. The nucleic acid and amino acid sequence of clone J7, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 19 and SEQ ID NO: 20, respectively).

Figure 24A-B. The nucleic acid and amino acid sequence of clone J8, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 21 and SEQ ID NO: 22, respectively).

Figure 25A-C. The nucleic acid and amino acid sequence of clone

J11 (SEQ ID NO: 23 and SEQ ID NO: 24, respectively).

Figure 26A-B. The nucleic acid and amino acid sequence of clone J14, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 25 and SEQ ID NO: 26, respectively).

Figure 27A-B. The nucleic acid and amino acid sequence of clone J15, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 27 and SEQ ID NO: 28, respectively).

Figure 28A-B. The nucleic acid and amino acid sequence of clone J16, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 29 and SEQ ID NO: 30, respectively).

Figure 29A-B. The nucleic acid and amino acid sequence of clone J17, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 31 and SEQ ID NO: 32, respectively).

Figure 30A-B. The nucleic acid and amino acid sequence of clone J19, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 33 and SEQ ID NO: 34, respectively). The amino acid sequence after the stop codon is given in SEQ ID NO: 54.

Figure 31A-B. The nucleic acid and amino acid sequence of clone J20, where the reading frame starts at nucleotide position 2 (SEQ ID NO: 35 and SEQ ID NO: 36, respectively).

Figure 32. SOUTHERN BLOT: Five micrograms of DNA isolated from 1. Human placenta, 2. NCI-H-1011 neuroblastoma cells, or 3. CHP 134 neuroblastoma cells were treated with the restriction enzyme A. Eco RI, B. Hind III, C. Bam HI, or D. Pst I, and then electrophoresed on an agarose gel and blotted onto a nylon membrane. The blotted

DNA was hybridized to the ^{32}P-labeled H3/H5 sequence. An autoradiograph of the hybridized blot is shown with the sizes of co-electrophoresed size markers noted in kilobases.

Added material is indicated by underlining.

1. (Amended) An isolated nucleic acid molecule encoding an odorant receptor protein, wherein the receptor protein comprises seven transmembrane domains and a 17-amino acid cytoplasmic loop between the fifth and sixth transmembrane domains, and is further characterized by at least one of the following characteristics:

(a) the loop between the first transmembrane domain and the second transmembrane domain, and the second transmembrane domain together comprise consecutive amino acids having the following sequence:
-L, X, X, P, M, Y, X, F, L- (SEQ ID NO: 55);

(b) the third transmembrane domain, and the loop between the third transmembrane domain and the fourth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-M, X, Y, D, R, X, X, A, I, C- (SEQ ID NO: 57); or

-D, R, X, X, A, I, C- (SEQ ID NO: 59);

(c) the loop between the fifth transmembrane domain and the sixth transmembrane domain, and the sixth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-K or R, X, F, S, T, C, X, S, H- (SEQ ID NO: 61); or

-F, S, T, C, X, S, H- (SEQ ID NO: 63); or

(d) the seventh transmembrane domain and the C-terminal domain together comprise consecutive amino acids having one of the following sequences:

-P, X, X, N, P, X, I, Y, X, L, R, N- (SEQ ID NO: 65); or

-P, X, X, N, P, X, I, Y- (SEQ ID NO: 67); or

-N, P, X, I, Y, X, L, R, N- (SEQ ID NO: 69);

wherein X is any amino acid.

6. (Amended) An isolated nucleic acid molecule encoding an odorant receptor protein comprising seven transmembrane domains and a 17-amino acid cytoplasmic loop between the fifth and sixth transmembrane domains, wherein the nucleic acid molecule encodes a protein selected from the group consisting of:

(a) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with tyrosine at position 333 as set forth in row F3 of Figures 4A to 4M (SEQ ID NO: 71),

(b) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with glutamine at

position 313 as set forth in row F5 of Figures 4A to 4L (SEQ ID NO: 72),

(c) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with lysine at position 311 as set forth in row F6 of Figures 4A to 4L (SEQ ID NO: 73),

(d) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with glycine at position 317 as set forth in row F12 of Figures 4A to 4L (SEQ ID NO: 74),

(e) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with leucine at position 310 as set forth in row I3 of Figures 4A to 4L (SEQ ID NO: 75),

(f) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with glycine at position 327 as set forth in row I7 of Figures 4A to 4L (SEQ ID NO: 76),

(g) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with tryptophan at

position 312 as set forth in row I8 of Figures 4A to 4L (SEQ ID NO: 77),

(h) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with leucine at position 314 as set forth in row I9 of Figures 4A to 4L (SEQ ID NO: 78),

(i) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with leucine at position 312 as set forth in row I14 of Figures 4A to 4L (SEQ ID NO: 79),

(j) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with leucine at position 314 as set forth in row I15 of Figures 4A to 4L (SEQ ID NO: 80), and

(k) an odorant receptor protein that shares from 40-80% amino acid identity with any one of the proteins of (a)-(j), comprises seven transmembrane domains, and is further characterized by at least one of the following characteristics:

(i) the loop between the first transmembrane domain and the second transmembrane domain, and the second transmembrane domain together comprise consecutive

amino acids having the following sequence: -L, X, X, P, M, Y, X, F, L- (SEQ ID NO: 55);

(ii) the third transmembrane domain, and the loop between the third transmembrane domain and the fourth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-M, X, Y, D, R, X, X, A, I, C- (SEQ ID NO: 57); or

-D, R, X, X, A, I, C- (SEQ ID NO: 59);

(iii) the loop between the fifth transmembrane domain and the sixth transmembrane domain, and the sixth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-K or R, X, F, S, T, C, X, S, H- (SEQ ID NO: 61); or

-F, S, T, C, X, S, H- (SEQ ID NO: 63); or

(iv) the seventh transmembrane domain and the C-terminal domain together comprise consecutive amino acids having one of the following sequences:

-P, X, X, N, P, X, I, Y, X, L, R, N- (SEQ ID NO: 65); or

-P, X, X, N, P, X, I, Y- (SEQ ID NO: 67); or

-N, P, X, I, Y, X, L, R, N- (SEQ ID NO: 69);

wherein X is any amino acid.

8. (Amended) An isolated nucleic acid molecule encoding an odorant receptor protein comprising seven transmembrane domains and a 17-amino acid cytoplasmic loop between the fifth and sixth transmembrane domains, wherein the nucleic acid molecule comprises a nucleic acid sequence which can be amplified by polymerase chain reaction using:

(a) any one of 5' primers A1 (SEQ ID NO: 37), A2 (SEQ ID NO: 38), A3 (SEQ ID NO: 39), A4 (SEQ ID NO: 40), or A5 (SEQ ID NO: 41); and

(b) any one of 3' primers B1 (SEQ ID NO: 42), B2 (SEQ ID NO: 43), B3 (SEQ ID NO: 44), B4 (SEQ ID NO: 45), B5 (SEQ ID NO: 46), or B6 (SEQ ID NO: 47).